Facts and Theories about Muscular Activity

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In modern physiology it is an axiom that any living structure or part of a structure must, either in itself or in co-operation with a specialised conducting mechanism, be capable of excitation, of response, and of conduction, if it is to play its part in the team which composes the whole organism. We sometimes forget that what now seems axiomatic was, in many cases, unheard of a few hundred years ago; and that a clear perception of our most valuable biological working principles has almost never burst upon the scientific world through the sudden illumination of some limpid genius, but has rather come into being as the descriptive epitome of a multitude of experiences which often appeared quite unrelated. It is humbling for us to realise that, so far as the growth of scientific knowledge is concerned, our business is merely to be excited, to respond, and to transmit: it is encouraging to be reminded that much of what seems meaningless at the first blush may, in the process of transmission, be changed into a typical example of some great principle.

In his *Fabrica Humani Corporis,* published in 1543, Vesalius first stated clearly that what passes along a nerve to excite a muscle passes by the substance, and not by the sheath of the nerve. And yet, beyond crude ideas about the flow of a nervous fluid, this great author had no understanding of conduction or excitability.

We notice an improvement in the conceptions of Borelli. In his posthumous life-work, published in 1679, we read: ". . . since the inflation, hardening, and contraction do not take place in the channels, . . . but take place outside the nerves, namely, in the muscles, . . . the influence which the nerves transmit is not of itself sufficient to bring about inflation. Something else must be added—something which is to be found in the muscles themselves." Borelli was in a fair way to appreciate the trigger-like action of the nerve in releasing the muscle's energy. During the ensuing century, despite a good deal of discussion, no very helpful conclusion was attained. And then, sometime not long before 1786, it so happened that Luigi Galvani was living in a house which had an iron railing round its balcony. One day Galvani chose to hang out a row of frogs from his balcony by means of copper hooks. To his astonishment the frogs, like so many marionettes, gave him a lively display of step-dancing. And from that historic moment there has been radiated all our modern knowledge of electricity. But the physicists must not be allowed to have Galvani all to themselves: he was a properly qualified medical man and a physiologist. He held that the movement of the muscles was due to the connection, by means of the metal contacts, of the positive charge within the nerve with the negative charge upon the exterior of the animal. It was Volta who recognised that the current was generated, not in the animal, but by the contact of the dissimilar metals. Volta's work led experimenters to devote their thought mainly to physical investigation, which was soon to be blessed with the names of Ampère, Ostwald, Ohm, Faraday, and their descendants.

Faraday, whose centenary occupied the scientific world last year, concerned himself with physiology so far as to give himself the customary shocks, and to 'convulse' the limbs of frogs, by means of the various sources of electrical energy. But his purpose in this was merely to prove that the electricity, whatever its source, was always the same in essence. Once he had established this, he does not appear to have been much interested in biology. Others, however, possessed of the new toys which the study of electro-magnetism provided for them, stimulated frogs' legs by the thousand, and amassed a huge store of information of a descriptive kind.

But while many great physiologists have been great chemists, not many have been great physicists. Already, in Faraday's time the growth of physiology was being stunted by an estrangement from her sister physics, which persisted until this century. Indeed, while the physical study of electricity was making phenomenal strides, the physiologists as a whole were far behind in ingenuity and exactness, a fact well exemplified by the study of the nervous impulse.

It was known that when a skeletal muscle was stimulated electrically, the length of time during which the current flowed did not appear to influence its efficacy. Further, when the current applied to the muscle was gradually increased to its maximum, instead of being instantaneously switched on, the muscle failed to respond by contraction. Smooth muscle, on the other hand, appeared to be quite contrary in its reactions. Duration of stimulus was evidently as important as intensity, while a progressively increasing current was as effective as the stimulus which the French so neatly term "brusque."

In the midst of the confusion, made worse by its supposed explanation in certain general "laws," there appeared the historic work of Du Bois Reymond, *Untersuchungen uber thierische Elektricitæt,* published in 1848. The author, whose work remained unchallenged for fifty years, formulated the celebrated law which bears his name. "Excitation," he said, "is a function of the differential co-efficient of the current density with respect to time." That is, whether a stimulus will succeed in exciting a given muscle to contract will depend upon the rate at which its strength increases when it is switched on.

This law, so convenient and far-reaching, was made to meet every emergency until Hoorweg the physicist, in 1892, and Weiss, in 1901, perceived its fallacies. Actually, they thought, skeletal muscle behaves in the same way as the smooth: a definite length of time must elapse between the arrival of an adequate stimulus at a muscle, and the beginning of the contraction. It is this length of time which is the true indication of excitability, and not the rapidity with which the current reaches the level where contraction will occur. Earlier workers had failed to appreciate this, because, in dealing with skeletal muscle, they had made no attempt to analyse the extremely short interval of time which comes between the stimulus and the response. This has been done most successfully by the methods of Lapicque, who, since 1903, has been working at the difficult subject of "chronaxie." Suppose that we had a method of stimulating a muscle for so long that the time factor need not be considered. Using this instrument, we could increase the strength of our shocks until the muscle began to show an answering contraction. This would give us a minimal value of stimulus which is called the "rheobase." Now, if we keep on stimulating the muscle at double the rheobase strength of shock, but gradually decreasing the length of time during which it acts, we shall find a minimum length of time below which the muscle will not respond. It is the minimum time which allows the muscle to respond to twice the rheobase stimulus which is called the "chronaxie." In actual practice, the very small lengths of time involved are measured by means of electrical condensers which have known times of discharge. These are used to give the shocks to the muscle.

Lapicque believed that he had proved that a muscle always had the same chronaxie as the nerve which supplied it—a principle known as "isochronism." Similar reasoning might be adopted to explain why an impulse travelling along the nervous system may successfully pass one synapse, and be stopped by another. Nerves having the same chronaxie could be regarded as "through routes" for a certain stimulus. Very recently, however, Rushton has complicated the picture by confirming what was suggested by Keith Lucas in 1906, namely, that a muscle may have more than one excitability, and therefore more than one chronaxie. There is no appearance of finality in this branch of study.

But the problems of the subject are being approached in numerous other ways. For example, in an instrument known as the Matthews oscillograph, the wireless valve amplifier has been harnessed to drive a special type of moving iron galvanometer. The photographic records obtained with this apparatus give a reasonably true graph of the minute currents which flow in a nerve during its natural activity. They do not, like the older records given by the capillary electrometer, need correction mathematically to make the amplitude of the recorded deflection a direct linear picture of the voltage which caused it. We can, for example, photograph the stream of discharges which is continually passing up the vagus nerve during life, or the volley of impulses which a single proprioceptive nerve-ending sends along its fibril when the muscle containing it is stretched. We have thus a powerful weapon at our disposal to attack the problem of how various factors influence conductivity and response. Thus it was used by Craib in 1930 to criticise the conventional explanation of the changes seen in electro-cardiographic records. In particular, he gives reason to abandon the view which regards active tissue as always electro-negative to inactive tissue. The actual potential, he holds, is purely a relative matter, and cannot depend merely upon the fact that a tissue is active. Incidentally, according to this theory, the much-debated "T" wave is of no more mysterious origin than the "Q-R-S" complex.

In a brief and superficial sketch of this kind, it would be foolish to catalogue the various theories which have been advanced in attempts to explain muscle activity. But we cannot conclude without a mention of the chemical approach to the problem, since it may yet prove to be the most productive of results. The whole matter is being constantly revised, but this much at least seems clear. Two metabolic processes are concerned in muscular activity—the one respiratory, requiring the presence of oxygen, and the other of the nature of ferment action, occurring anærobically. When the nervous impulse arrives at the muscle, the first happenings are anærobic. Glycogen, the main source of the muscle's energy, is broken down to lactic acid, and it is the presence of the latter which appears to be the causative agent in bringing about contraction. The recovery of the muscle, which must take place during the "refractory period," when the muscle will not respond to further stimulation, requires the presence of oxygen. Of the lactic acid formed during activity, about four parts are built up again to glycogen, while one part is burnt up to carbon dioxide and water.

In addition to the carbohydrate changes in the muscle, there are other less evident, but equally important, changes during the action. Thus there are the comparatively slow operations of the complex nucleotide mechanism, without which the glycogen cannot be hydrolysed. There are also the essential and very rapid changes undergone by the labile compound between creatin and phosphoric acid, which can be ærobically built up in the normal muscle.

How the nervous impulse is related to these chemical happenings may become clear before many years; and the clinical importance of such a discovery would doubtless be great. There would, for instance, be a rational basis for the consideration of the myopathies, where the disturbance of function occurs outside the nervous system; while we could hope for light upon the cause of the rapid fatigue of muscle seen in myasthenia gravis, and even upon the very practical problem of occupational palsies.

Already one of the complex nuclear derivatives referred to has been placed on the market as a dilator of the coronary vessels. Whether the claims made for its value in coronary occlusion will be substantiated, remains to be seen. In any event, the study of muscular action must always be of moment to the clinician, for however little we may employ the muscles of our limbs, there is no living if the heart should cease its work.

BRITISH MEDICAL ASSOCIATION—BELFAST DIVISION

THE annual meeting of the Division was held in the Medical Institute on Thursday, 12th May, 1932. The chairman, Dr. Robert Marshall, presided. Dr. S. R. Hunter, Dunmurry, was elected chairman for the ensuing year, and Dr. G. G. Lyttle, Belfast, was elected vice-chairman. The Division congratulates Dr. J. C. Loughridge on his election as member of the Council of the British Medical Association, in place of the late Dr. R. W. Leslie, whose loss we deeply deplore as one who faithfully served the Association for many years. Dr. Loughridge was one of our representatives at the annual representative meetings, and his reports to the Division showed the interest and enjoyment he derived from his work. His promotion to the inner circle of the British Medical Association is a well-deserved honour. The Division welcomes our new representative, Dr. H. J. Ritchie, Belfast, who has long taken a prominent part in all that makes for the welfare of the profession. It was suggested that next session should open with a discussion on "The Future of Medical Practice." The extension of the Public Health Services